0099 CYTOMORPHOLOGIC AND MORPHOMETRIC STUDIES OF HEPATOCARCINOGENESIS. II. REVERSIBILITY OF NUCLEAR SIZE ALTERATIONS OCCURRING IN THE NITROSOMORPHOLINE-TREATED RAT LIVER. *(Ger.)* Romen, W. (Inst. Path. U. Würzburg, Germany), W. Ross and P. Bannasch. *Z Krebsforsch* 73:134-140, 1972.

The morphometry of 73 male Sprague-Dawley rat hepatocyte nuclei was studied after a 7 wk treatment period with nitrosomorpholine (12 mg/100 ml drinking water/day) and 4, 52 and 87-97 weeks after the end of the feeding period. Attention was focused on 4 cell categories referred to as glycogen-poor, "clear" glycogen storage, hepatoma, and hepatocyte population remainder cells, referred to as X-cells. The nuclear area of non-treated rat liver cells reached peak values ranging from 45 to 50 μm^2. Nuclear enlargement to double the normal size was observed in the X-cells and most of the glycogen-storage cells, at the end of the 7 wk treatment period. More than 30% of the X-cells and 25% of the glycogen storage cells had triple nuclear volumes. The glycogen-poor cell nuclei were also enlarged, but to a lesser extent. Four weeks later, a minor regression of the nuclear enlargement was observed in the glycogen storage and some of the X cells, while total disappearance of the glycogen-poor cells occurred. Both glycogen storage and X-cell nuclei returned to normal size 52 wk after the end of carcinogen intake; scattered hepatoma cells and small hepatoma cell clusters were observed. Eighty seven wk after the end of experimental treatment period both storage and X cell nuclei remained unaltered with respect to the observations recorded 52 wk post treatment. Large numbers of hepatoma cells with 75 μm^2-100 μm^2 nuclei, the latter comparable in size to those seen at the end of the acute poisoning stage, were observed, 87 to 97 wk after the end of the carcinogen intake period. Nuclear enlargement occurring in hepatocytes after carcinogen intake should be viewed differently than that in hepatoma cells. The initial nuclear enlargement occurring as a result of toxic effects was found to be a reversible phenomenon and therefore cannot be considered as a precancerous cell reaction. Post treatment studies rather than long-lasting treatment experiments are recommended to clarify the karyologic events related to carcinogenesis.

0100 FOLATE DEFICIENCY AND FORMIMINOGLUTAMIC ACID EXCRETION DURING CHRONIC DIETHYLNITROSAMINE ADMINISTRATION TO RATS. *(E.)* Poirier, L. A. (Montreal Cancer Inst., Quebec, Canada) and V. M. Whitehead. *Cancer Res* 33(2): 383-388, 1973.

Elevated levels of the histidine catabolite formiminoglutamic acid were excreted into the urine of male Wistar rats given both 0.01% diethylnitrosamine in their drinking water for 1-5 wk and an injection of a loading dose of histidine. Similar histidine loading of control rats that received no carcinogen did not produce an elevation in urinary formiminoglutamic acid excretion. The elevation in urinary formiminoglutamic acid excretion caused by chronic diethylnitrosamine administration was prevented by high dietary levels of the methyl donors methionine, betaine, and choline; high dietary levels of folate and vitamin B_{12}, either alone or in combination, had no significant effect on the elevated formiminoglutamic acid excretion caused by diethylnitrosamine. The elevated formiminoglutamic acid excretion caused by the administration of diethylnitrosamine for 3 wk was associated with a decrease in the hepatic levels of the enzymes formiminoglutamic acid transferase and urocanase, and with a decreased hepatic content of the higher conjugates of folate. Whereas dietary methionine administration completely prevented this decrease in the hepatic content of the higher conjugates of folate, dietary folate had no effect. Diets that contained elevated levels of methionine and choline also led to only a slight reversal of the decreased hepatic formiminoglutamic acid transferase activity caused by diethylnitrosamine. Thus the antagonistic effects on formiminoglutamic acid excretion by diethylnitrosamine and the methyl donors appeared to be mediated through the hepatic content of folic acid cofactors.

0101 INTERACTION OF 4-NITROQUINOLINE 1-OXIDE AND RELATED CARCINOGENS WITH HISTONE AND ALIPHATIC AMINO ACIDS. *(E.)* Okano, T. (Pharmaceutical Inst., Tohoku U., Japan) and Y. Sato. *Gann* 63(6):713-724, 1972.

Examinations were made on the interaction between carcinogenic quinoline derivatives and calf thymus histone, and 13 of its constituent aliphatic amino acids. The interaction systems of histone and quinolines produced a difference spectrum in the visible region and intensity of this difference spectrum increased by heat denaturation of histone. The 13 aliphatic amino acids were classified into three kinds by the manner of their interaction with quinolines; glycine, alanine, leucine, isoleucine, valine, glutamic acid, and aspartic acid did not show any tendency to interact with the quinolines. Arginine, lysine, and proline, which have basic group with p*Ka* larger than 10, produced a new absorption band in the visible spectral region which did not change with time. Methionine, serine, and threonine, which have a nucleophilic group in their molecule, produced a visible difference spectrum by interaction with the quinolines and the spectral intensity increased with time. The complexes formed between basic amino acids and 4-nitroquinoline 1-oxide were analyzed on the basis of Benesi-Hildebrand formula. It was concluded that an n-π charge transfer between quinolines and basic amino acid moiety of the macromolecule played an important part in the intermolecular interaction between the quinolines and histone.